Glucose, Fatty Acid, and Urea Kinetics in Patients with Severe Pancreatitis

The Response to Substrate Infusion and Total Parenteral Nutrition

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Rates of glucose turnover and oxidation in normal volunteers (N = 16) and in severely ill patients with pancreatitis (N = 9) were isotopically determined. Glucose turnover was determined using primed constant infusions of either 6-^{3}H-glucose or 6-d_2-glucose, and glucose oxidation with either U-^{14}C-glucose or U-^{13}C-glucose after appropriate priming of the bicarbonate pool. Urea kinetics were determined using primed constant infusions of either ($^{15}N_2$)-urea or U-^{14}C-urea, whereas free fatty acid (FFA) kinetics were determined by the constant infusion of 1,2-^{13}C palmitate. Basal rates of glucose production and plasma glucose clearance were significantly higher in the patients than in the volunteers. During glucose infusion (4 mg/kg/min) endogenous glucose production was virtually totally suppressed in the volunteers (94 ± 4%). There was significantly less suppression in the patients, however (44 ± 1%). In addition, the percentage of available glucose oxidized (*i.e.*, percentage of uptake oxidized) was significantly less in the patients than in the volunteers. The basal rate of urea production was significantly higher in the patients; however, in both patients and volunteers, glucose infusion resulted in a significant decrease. The rate of FFA turnover was similar in the patients and volunteers, and the patients and volunteers were equally sensitive to the suppressive effects of glucose infusion. When the patients were studied during total parenteral nutrition (TPN), there was no further suppression of endogenous glucose turnover than that seen during 2 hours of glucose infusion, and the mean rate of urea turnover measured during TPN (7.0 ± 1.9 μmol/kg/min) was also not significantly different than the value determined during glucose infusion (8.9 ± 1.8 μmol/kg/min). It was concluded from these studies that patients with pancreatitis (1) are metabolically similar to septic patients, (2) have an impairment in their ability to oxidize infused glucose when compared with normal volunteers, (3) have an elevated rate of net protein catabolism, and (4) have FFA kinetics similar to those seen in normal humans.

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GLUCOSE INFUSION MAY BE BENEFICIAL to the host for two major reasons. First, the infused glucose may induce a suppression of endogenous glucose production, thereby sparing gluconeogenesis from protein and conserving body reserves.[1] Second, the infused glucose may be directly oxidized for energy.[2] It is likely that glucose infusion either alone or as part of a parenteral feeding regimen is beneficial in patients with pancreatitis. However, few studies have specifically addressed glucose metabolism in patients with pancreatitis. It has been suggested that pancreatitis patients are metabolically similar to seriously septic individuals[3]; however, this is not an established fact. Furthermore, there is debate as to whether nutritional support results in either conservation of bodily resources or an influence on the clinical outcome of patients with pancreatitis.[4]

Long et al.[5] have suggested that in contrast to what is seen in normal individuals, glucose infusion does not suppress endogenous glucose production in septic patients. However, in a previous study we observed that glucose infusion in septic patients resulted in some suppression of both endogenous glucose turnover and protein breakdown, but to a more limited extent than in normal volunteers.[6] The ability of septic patients to oxidize glucose (both endogenous and infused) has also been widely studied. Some investigators suggest that the ability of septic patients to oxidize glucose is greater than that seen in normal individuals,[7] whereas others have concluded that there is either a decrease[8] or no change.[6,9] The situation regarding the ability of the patient with pancreatitis to oxidize glucose is not known. In addition, fat metabolism and the response of glucose and protein metabolism in

TABLE 1. *Clinical Details of Pancreatitis Patients*

Patient Number	Sex	Age	Diagnosis	Treatment	Outcome
1	M	37	Pancreatitic fistula (traumatic)	Drainage	Died
2	M	71	Odematous pancreatitis (2 degrees to penetrating duodenal ulcer)	Resection	Died
3	M	80	Hemorrhagic pancreatitis (gallstones)	Conservative	Survived
4	M	60	Hemorrhagic pancreatitis (alcoholism)	Conservative	Died
5	M	50	Hemorrhagic pancreatitis (alcoholism)	Conservative	Survived
6	M	60	Hemorrhagic pancreatitis (2 degrees perforated duodenal ulcer)	Conservative	Survived
7	F	50	Hemorrhagic pancreatitis (ideopathic)	Drainage	Died
8	F	82	Odematous pancreatitis (ideopathic)	Drainage	Survived
9	M	60	Hemorrhagic pancreatitis (alcoholic)	Conservative	Died

pancreatitis patients to total parenteral nutrition (TPN) has not been determined isotopically.

Because of the uncertainties concerning these metabolic responses in pancreatitis patients, we performed a series of studies in an attempt to clarify these problems. We determined rates of glucose, fatty acid, and urea turnover and glucose oxidation in normal volunteers (N = 16) and in pancreatitis patients (N = 9). Studies were performed in the basal state, during glucose infusion (4 mg/kg/min), and during TPN.

Patients and Methods

Studies were performed in 16 normal volunteers and in nine patients with acute pancreatitis. All patients were hemodynamically stable, and no patients were receiving either pressor or ventilatory support at the time of the study. When the patients were studied in the basal state they were not receiving any glucose intravenously, and all patients were at least 12 hours postabsorptive. Four of the pancreatitis patients were studied within 1 week of surgical intervention, and the other five patients were studied either before operation or they were nonoperative patients. The patients studied during TPN had had no oral intake for at least 4 days. The volunteers were all men and varied in age from 18–37 years. They were considered normal on the basis of not having any significant medical history and having normal findings on a physical examination done at the time of the study.

TABLE 2. *Details of Total Parenteral Nutrition*

Patient Number	Age	Glucose Infusion rate μmol/kg/min	Lipid Infusion (ml 20% lipid/d)	Nitrogen Intake (g/d)
2	71	22.0	600	16.0
3	80	27.5	650	17.6
6	60	20.0	800	16.0
8	82	22.9	600	16.0
Mean		23.9 ± 1.5	660 ± 37.0	16.6 ± 3.9

The Institutional Review Board at Auckland Hospital approved the study. Despite the high mortality rate of the group at the time of the study, each patient gave informed consent before the study. Radiation safety approval was obtained from the National Radiation Laboratory.

The clinical details of the patients are summarized in Table 1. The TPN data are shown in Table 2. The patients studied during TPN received approximately 50% of their calories as glucose and 50% as fat, with a mean nitrogen intake of 17.6 ± 2.5 g/d (see Table 2).

Study Design

Glucose turnover–oxidation studies. Glucose turnover–oxidation studies were performed over a 4-hour period and isotopes were infused throughout. During the first 2 hours (Period I) isotopes alone were infused, and throughout Period II (2 hours duration) glucose was also infused (at approximately 20 μmol/kg/min). Isotopes were infused through one venous line, and plasma samples for measurement of isotopic specific activity were collected either from an arterial line if one was present, or from a separate venous catheter. Frequent plasma samples were collected during the last half hour of Period I and again during the last half hour of Period II. Oxygen consumption (V_{O_2}), carbon dioxide production (V_{CO_2}), and respiratory quotient (RQ) were determined during Period I and Period II. In addition, during the last half hour of each period, expired air samples were collected in 6-L anesthetic bags for determination of $^{14}CO_2$ specific activity.

Fatty acid turnover studies. Fatty acid turnover studies were also performed over a 4-hour period. During Period I (2 hours duration) 1,2^{13}C-palmitic acid was infused at 0.02 μmol/kg/min (no prime). In Period II the isotopic infusion was continued, and either glucose was infused (20 μmol/kg/min) or, alternatively, in the "control" protocols there was no perturbation.

Urea turnover studies. In the volunteer group the stable isotope ($^{15}N_2$)-urea was used to determine urea turnover, thereby avoiding any radiation hazard. In the patients

urea turnover was determined using ^{14}C-urea. In both groups primed constant infusions were used, and the study design was similar to that used for the glucose turnover–oxidation protocols, except that Period I was extended to 3 hours to ensure that an isotopic equilibrium was obtained in the urea pool[2,6] (see Table 3).

TPN studies. The study design used for TPN studies was similar to that described above. However, in these studies the experiments ended after the completion of Period I since glucose was being infused in Period I.

TABLE 3. *Indirect Calorimetry Data for Volunteers and Patients*

	V_{CO_2}	V_{O_2}	RQ
Normal volunteers			
Basal	85 ± 14	126 ± 19	0.77 ± 0.02
Glucose infusion	93 ± 14	125 ± 20	0.81 ± 0.03*
Pancreatitis patients			
Basal	125 ± 5†	170 ± 6†	0.73 ± 0.02
Glucose infusion	123 ± 16	165 ± 29	0.71 ± 0.02†
TPN	135 ± 6	151 ± 4	0.90 ± 0.01

* Significantly different from basal value ($p < 0.05$).
† Significantly different from equivalent volunteer value ($p < 0.05$).

Isotopic Infusions

Glucose turnover–oxidation studies. In all instances, and either 6,6-d_2- or 6-^{3}H-glucose and either U-^{13}C- or U-^{14}C-glucose were administered as prime constant infusions throughout the study. The isotopic infusion rates were 1 nCi/kg/min for each radioisotope. The infusion rates for 6,6-d_2-glucose and U-^{13}C-glucose were 0.05 mg/kg/min and 0.002 mg/kg/min, respectively. The priming dose: infusion ratio was 80:1 for each isotope, and the bicarbonate pool was primed with either 0.18 uCi/kg of $NaH^{14}CO_3$ or 0.16 mg/kg of $NaH^{13}CO_3$ given over 1 minute at the onset of the study.

Urea and palmitate turnover studies. The infusion rates were as follows. U-^{14}C urea: infusion rate = 0.5 nCi/kg/min, prime = 225 nCi/kg. ($^{15}N_2$)-urea: infusion rate = 0.03 mg/kg/min, prime = 13.5 mg/kg. 1,2-^{13}C-palmitate infusion rate = 0.02 μmol/kg/min.

Sample Analysis

Blood samples were immediately chilled and then centrifuged to separate the plasma.

Glucose-specific activity. One-milliliter plasma samples were used for the determination of glucose-specific radioactivity as we have described before.[9]

Plasma glucose enrichment. Determination of ^{13}C-glucose enrichment was done by means of isolation, combustion, and analysis by isotope ratio mass spectroscopy (IRMS) as described previously.[2]

When glucose kinetics were determined by infusing 6,6-d_2-glucose as the tracer, isolation was similar to that for ^{13}C-glucose, but the analysis of the glucose enrichment was performed by gas chromatography mass spectrometry (GCMS) using a penta-acetate derivative.[9] Ions at m/e 331 and 333 were used in the chemical ionization mode for selected ion monitoring using a GCMS system.[9] The comparison between glucose kinetics calculated by ^{3}H- and 6,6-d_2-labeled glucose and U-^{13}C- *versus* U-^{14}C-glucose has been published previously.[2,9]

Urea turnover. ^{14}C-urea turnover was determined using the method of Wolfe.[10] After precipitation of proteins, samples were diluted 1:4, and after incubation at 40 C with urease for 20 minutes, phenol was added, followed by hypochloride solution. After incubation at 70 C for 20 minutes the samples were cooled and absorption was determined spectrophotometrically at 650 nm. Urea concentration was then determined using a standard curve. A 250-mL sample dissolved in 10 mL of scintillation cocktail was then counted for radiation content using a beta liquid scintillation counter. From these data urea-specific radioactivity was calculated.

^{15}N-urea. Urea enrichment was determined by GCMS analysis using the N,N^1-bis-trimethyl derivative of urea. Urea rate of appearance calculated by (^{15}N)-urea *versus* U-^{14}C-urea has been published previously.[9,10]

1,2-^{13}C-palmitate. Palmitate acid enrichment was determined by GCMS analysis as described previously.[9] Palmitic acid and total FFA concentration were quantitated on a gas chromatograph using heptadecanoic acid as an internal standard.[9]

Expired air $^{14}CO_2$ specific activity. $^{14}CO_2$ specific activity was determined by trapping expired air in a solution of hyamine-hydroxide using 0.1% phenolphthalein solution as an indicator. The 0.1% phenolphthalein solution was mixed with hyamine-hydroxide and absolute alcohol in a ratio of 1:5:9. Three-milliliter samples of the solution were then used to trap 1.0 mmol of CO_2. The vials containing the trapped CO_2 were then mixed with 15 mL of scintillation cocktail and counted on a beta liquid scintillation counter.[9]

Expired air $^{13}CO_2$ enrichment. Expired air was collected in 6-L anesthesia bags using a three-way valve. The air was then bubbled through 0.1N NaOH to trap the CO_2. The trapped gas was later liberated in an evacuated Rittenberg tube by the addition of concentrated (85%) phosphoric acid, and the atoms per cent excess (APE) was then determined on an isotope ratio mass spectrometer.[2]

Indirect Calorimetry

Indirect calorimetry was performed using a Sybron Taylor (UK) oxygen analyzer and an ADC CO_2 analyzer (Hertsfordshire, England).

TABLE 4. *Rate of Net Protein Catabolism* (mg protein/kg/hr)

	Volunteers	Pancreatitis Patients
Basal	60 ± 6	102 ± 19†
Glucose infusion	52 ± 6*	93 ± 18*†

* Significantly different from basal value ($p < 0.01$).
† Significantly different from volunteer value ($p < 0.05$).

Calculations

Isotopic Calculations

Glucose rate of appearance (production), urea rate of appearance, and glucose oxidation were all calculated using standard formulas.[9]

To calculate glucose oxidation, the percentage of recovery of bicarbonate had to be determined.[9] We have previously shown that in normal volunteers, 75% of infused carbon is recovered in expired air (K = 0.75).[2,9,10]

In the patients, we could not assume that the value for the percentage of recovery of bicarbonate would be the same as for the volunteers. We therefore performed 16 $NaH^{14}CO_3$ infusions to determine bicarbonate recovery in "stressed humans." $NaH^{14}CO_3$ was infused at 1 nCi/kg/min with a priming dose of 80 nCi/kg.

The recovery of infused $NaH^{14}CO_3$ as $^{14}CO_2$ was higher in the patients than in the volunteers, and the percentage of recovery was proportioned to the V_{O_2}. Using a linear regression analysis, we determined the mathematical expression for this correlation. This equation was used to calculate the exact K value for each patient, both in the basal state and during glucose infusion (see Results).

Urea Rate of Appearance

Radio-urea (^{14}C). Here, urea rate of appearance was calculated according to the Steele equation[11]:

$$RA = \frac{F}{SA}$$

F = isotopic infusion rate (dpm/kg/min). SA = ^{14}C-urea plasma specific activity.

($^{15}N_2$)-urea. Total urea production (Ra_T) is equal to the urea produced from recycled nitrogen (Ra_R). Ra_T is calculated by a slight modification of the Steele equation[11]:

$$Ra_T = \left(\frac{^{IE}F}{B} - I\right) \times F$$

F is the urea infusion rate (μmol/kg/min); ^{IE}F is the isotopic enrichment (mole per cent excess, MPE) of (^{15}N)-urea infusate; and B is the enrichment (MPE) of the molecular fragment of m − 191 (A + 2) of plasma urea.

The comparison of the urea turnover calculated by ^{14}C-urea *versus* ($^{15}N_2$)-urea is described by Wolfe.[9,10]

Palmitate turnover. Palmitate turnover is calculated by the following equation:

$$\text{Palmitate Ra}\,(\mu\text{mol/kg/min}) = \left(\frac{^{EI}i}{IE} - 1\right) \times F$$

where ^{IE}i and ^{IE}p are the isotopic enrichments of the infusate and plasma (atom per cent excess, APE) respectively.

For the calculation of FFA kinetics using 1,2-^{13}C palmitate we have assumed that the metabolism of palmitate is representative of all fatty acids. Therefore:

$$\text{Ra of total FFA} = \frac{\text{Ra (palmitate)}}{\%\ \text{palmitate}} \times 100$$

where % palmitate = the percentage of the total FFA concentration that is composed of palmitate. We have described this method before.[12]

Net protein catabolism. Net protein catabolism was calculated from the urea turnover data as described previously.[9]

Statistical Analysis

The equilibrium turnover and oxidation data obtained for each subject during the last half hour of Period I were compared with the corresponding value obtained during Period II by means of a paired t-test. An analysis of variance was used to compare data among the various groups, and a linear regression analysis was used to calculate the relationship between the V_{O_2} and the percentage of recovery of bicarbonate in the expired air.

Rates of glucose infusion and TPN details. The mean rate of glucose infused during Period II was 20.5 ± 1.0 μmol/kg/min (3.7 ± 0.2 mg/kg/min). The mean rate of glucose infusion in Period II was 23.0 ± 0.5 μmol/kg/min (not significantly different from the infusion rate in volunteers). During TPN the mean glucose infusion rate was 27.5 ± 2.5 μmol/kg/min (4.95 ± 0.4 mg/kg/min).

Results

The subjects (volunteers and patients) were not obviously affected physiologically by the infusion of the isotopic solutions, and the volumes of blood removed for sampling approximated the volume of fluid infused.

The calorimetric data for the volunteers and patients are summarized in Table 2. The basal V_{CO_2} and V_{O_2} values were significantly higher in the patients ($p < 0.05$) than in the volunteers. The RQ increased during glucose infusion in the volunteer group ($p < 0.05$) but not in the patients (see Table 4).

In the "control" protocols when isotopes alone were infused for the duration of the study, there was no change in specific activity (radioisotopes) or in plasma enrichment

(stable isotopes) between Periods I and II. These data are summarized in Figure 1. Since no changes in isotopic abundance occurred between Periods I and II in these "control" studies, in the various "test protocols" in which the system was perturbed during Period II, we have statistically compared the data obtained in Period I with that obtained in Period II in the same group.

Basal Glucose Kinetics and the Response to Glucose Infusion

The basal values for plasma glucose concentration were similar in the patients and volunteers (5.1 ± 0.1 and 5.2 ± 0.2 μmol/ml, respectively). After glucose infusion in Period II the plasma glucose concentration rose significantly in both groups. The absolute plasma glucose level during glucose infusion was higher in the patients, but this did not reach statistical significance (Fig. 2). The basal rate of glucose production was significantly higher in the patients (23.9 ± 4.0 *versus* 13.9 ± 0.3 μmol/kg/min, respectively, $p < 0.01$). When the volunteers were infused with glucose in Period II, endogenous glucose production was virtually abolished (94 ± 4% suppression), but in the patients, glucose infusion induced a suppression of only 45 ± 1%—significantly different from the volunteer group ($p < 0.05$) and different from the basal patient value ($p < 0.01$). The rate of glucose clearance from the plasma was also significantly higher in the patients ($p < 0.01$). The values were 5.0 ± 1 and 2.8 ± 0.1 mL/kg/min for patients and volunteers, respectively (see Fig. 2).

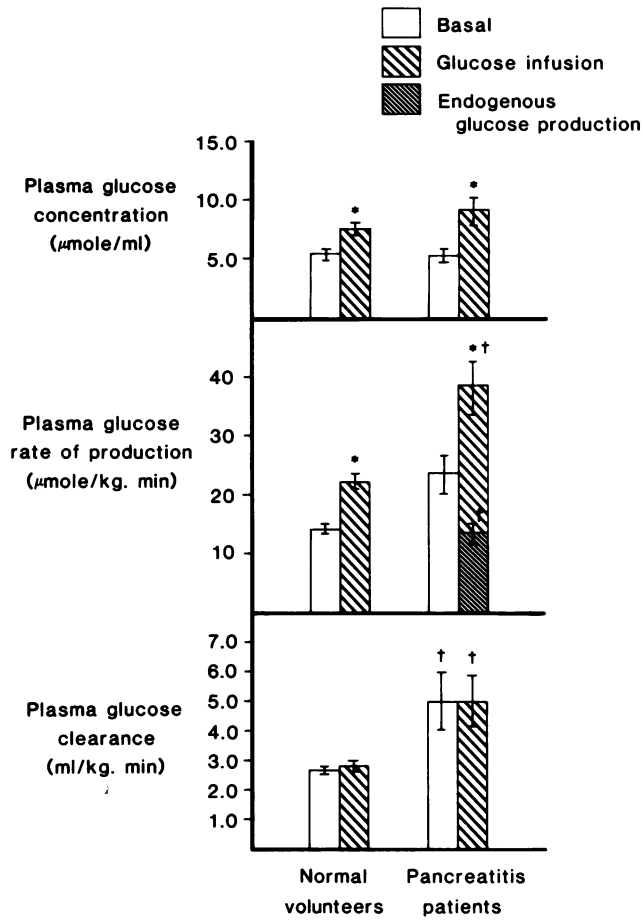

FIG. 2. Plasma glucose concentration data and glucose kinetics in volunteers and pancreatitis patients—basal data and the response to glucose infusion. Asterisk denotes value significantly different from the equivalent basal value ($p < 0.01$). Dagger denotes value significantly different from the equivalent volunteer value ($p < 0.05$). Values are mean ± SEM.

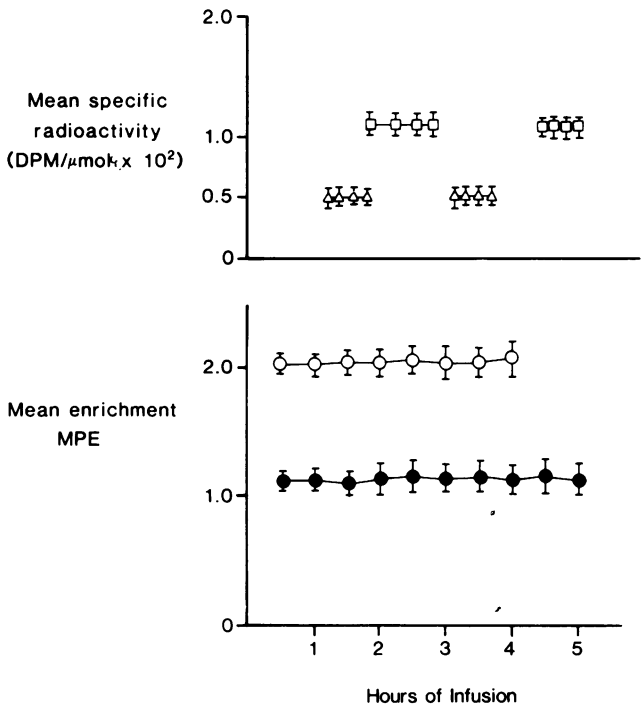

FIG. 1. Average enrichments (MPE) of five volunteers and five patients infused with only tracer doses of isotopes for the entire experimental period. (● —— ●) = $^{15}N_2$-urea (0.59 μmol/kg/min); (□ —— □) = U-^{14}C-urea (1 nCi/kg/min); (○ —— ○) = 6-d_2-glucose (0.044 mg/kg/min); (△ —— △) = 6-^{3}H-glucose (1 nCi/kg/min). Values are mean ± SEM.

In both the basal state and during glucose infusion, the rates of glucose oxidation were higher in the patients, although the differences were not statistically significant (Fig. 3). In the basal state the percentage of available glucose that was oxidized (*i.e.*, percentage of glucose uptake oxidized) was similar for volunteers and patients. However, when glucose was infused in Period II the percentage of glucose uptake oxidized decreased significantly ($p < 0.05$) in the patient group (see Fig. 3).

Bicarbonate Recovery

The $NaH^{14}CO_3$ infusion data showed a positive correlation between the V_{O_2} and the percentage of recovery of bicarbonate. From these data an equation to calculate

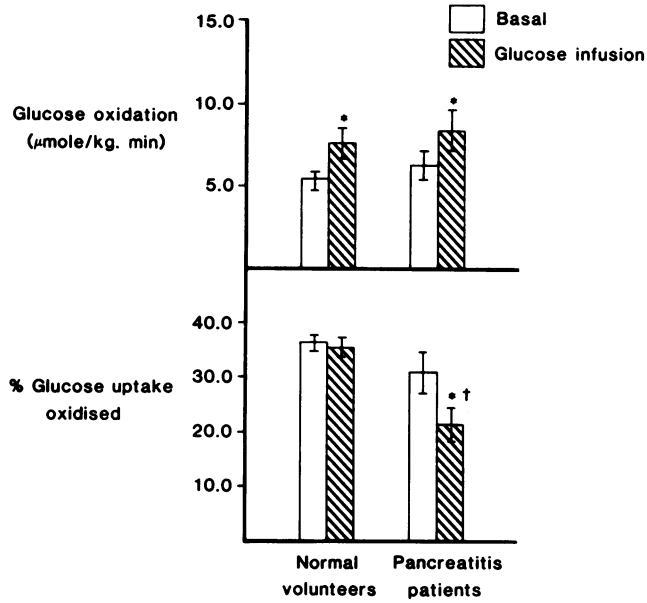

FIG. 3. Glucose oxidation data in volunteers and pancreatitis patients—basal data and the response to glucose infusion. Asterisk denotes value significantly different from the equivalent basal value ($p < 0.01$). Dagger denotes value significantly different from the equivalent volunteer value ($p < 0.05$). Values are mean ± SEM.

percentage recovery from the VO_2 was deduced as follows (see Fig. 4):

$$K = 61.7 + (0.2 \times VO_2)$$

Basal Urea Kinetics and Response to Glucose Infusion

The basal urea concentration in the patients was significantly higher than in the volunteers ($p < 0.05$). When glucose was infused, the plasma urea concentration decreased in both groups although this reached statistical significance only in the patients ($p < 0.05$; see Fig. 5). The rates of urea production were significantly higher in the patients, both in the basal state and during glucose infusion. However, in both volunteers and patients, glucose infusion resulted in a significant decrease in urea production ($p < 0.01$ in the volunteers and $p < 0.05$ in the patients see Fig. 5).

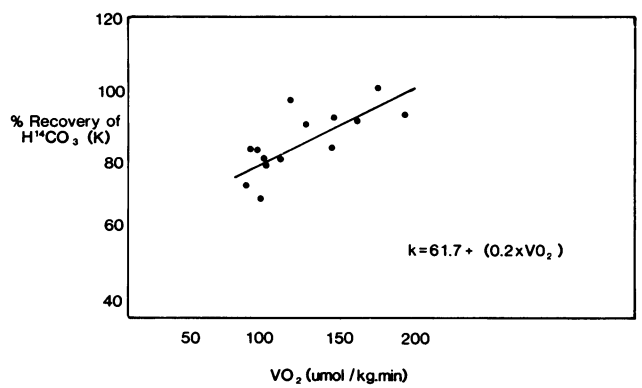

FIG. 4. Percentage recovery of infused $NaH^{14}CO_3$ as $^{14}CO_2$. Circles represent individual data points.

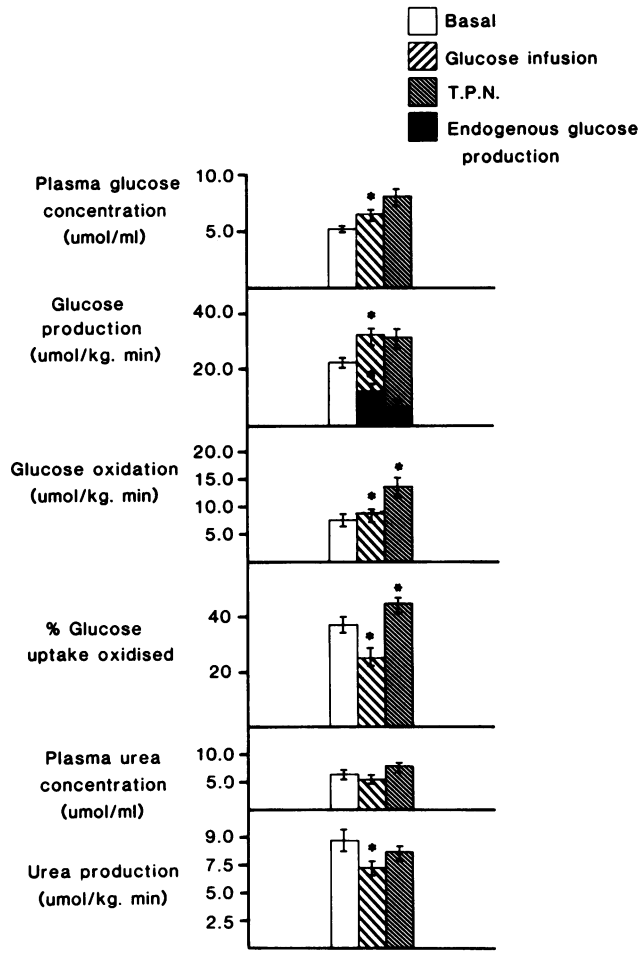

FIG. 5. The effect of TPN on glucose and urea kinetics in pancreatitis patients compared with the responses in the basal state and during glucose infusion. Asterisk denotes value significantly different to preceding value ($p < 0.05$).

The rate of net protein catabolism in the patients was significantly higher than in the volunteers, but glucose infusion resulted in a significant decrease in both groups (see Table 4).

Basal Palmitate Kinetics and the Response to Glucose Infusion

The basal rates of appearance for palmitate and FFA in the volunteers were 1.7 ± 0.3 and 6.5 ± 0.8 μmol/kg/min, respectively. The corresponding values in the patients were 1.4 ± 0.4 and 4.2 ± 1.4 μmol/kg/min, respectively. After glucose infusion, the rates of palmitate and FFA turnover decreased significantly in both volunteers and patients ($p < 0.05$, see Table 5). When glucose was not

infused in Period II (control studies), turnover data obtained in Periods I and II were not significantly different.

Glucose and Urea Kinetics During TPN

The effects of TPN on glucose and urea kinetics are shown in Figure 5. The effects of TPN beyond those of glucose infusion alone were: (1) no further suppression of endogenous glucose production, (2) a marked increase in the percentage of glucose uptake oxidized with a consequent increase in glucose oxidation, and (3) no significant change in either the plasma urea concentration or the rate of urea production.

TABLE 5. *Free Fatty Acid Kinetics in the Basal State and During Glucose Infusion*

	Volunteers		Pancreatitis Patients	
	Basal	Glucose Infusion	Basal	Glucose Infusion
Palmitate rate of appearance (μmol/kg/min)	1.7 ± 0.3	1.1 ± 0.2*	1.4 ± 0.4	0.9 ± 0.3*
FFA rate of appearance (μmol/kg/min)	6.5 ± 0.8	3.5 ± 0.7*	4.2 ± 1.4	3.0 ± 1.0*

* Significantly different from basal value ($p < 0.05$).

Discussion

The limited suppressibility of endogenous glucose production in pancreatitis patients is in general agreement with our previous observations in septic patients.[6] This finding extends the observation of Long et al.[5] who only assessed the response to a low dose (1 mg/kg/min) glucose infusion in severely ill patients. Also of interest is the failure of TPN to suppress endogenous glucose production further than that seen with 2 hours of glucose infusion. In the volunteers, glucose infusion alone virtually abolished endogenous glucose production, a finding we have observed previously.[6]

These data are consistent with the recent observations made by Streat and colleagues[13] using *in vivo* neutron activation analysis in patients with pancreatitis and sepsis. They found that despite the provision of amounts of protein and calories adequate to meet metabolic demands, severely ill septic patients still lost up to 20 g of nitrogen daily. Patients with pancreatitis were generally less severely affected, but in these patients also it was difficult to reverse the accelerated protein breakdown.[13,14] The urea turnover data and the net protein catabolism results in the current study are consistent with these findings. When the pancreatitis patients were infused with glucose their protein losses decreased significantly, but despite this the mean rate of net protein catabolism in the patients during glucose infusion was still much higher than that seen in the volunteers in the basal state. On the other hand, although the patients with pancreatitis had enhanced rates of protein breakdown and limited suppression after substrate infusion, those changes are not as impressive as might have been predicted when one considers the marked negative state of nitrogen balance that has been reported in similar groups of severely stressed patients.[4,15] Therefore, it appears likely that patients with pancreatitis also have an associated impairment in the capacity for net protein synthesis.

The enhanced rate of glucose clearance seen in the patients with pancreatitis, both in the basal state and during glucose infusion, is also consistent with the premise that these patients are metabolically and nutritionally similar to septic patients. A number of observations by others in animals[16] and also by ourselves in both septic animals[12] and septic patients[6] have established that an enhanced rate of plasma glucose clearance is a metabolic characteristic of sepsis. This in part reflects the metabolism of the inflammatory tissue associated with the septic process. It may also be due to a systemic effect.

The significant decrease in the percentage of glucose uptake oxidized that was seen in the pancreatitis patients during glucose infusion is consistent with the general principle that the processes of metabolic regulation are rendered less efficient in critical surgical illness.[6,12,17] However, this decreased capacity of the patients to oxidize infused glucose increased greatly during TPN, rising above the value seen in normal volunteers during glucose infusion. The indirect calorimetric data are in general agreement with the isotopic data with respect to an impairment on the part of the pancreatitis patients to oxidize infused glucose during the 2 hours of glucose infusion. The RQ increased significantly in the volunteers after glucose infusion (0.77 ± 0.02 to 0.81 ± 0.03), whereas in the patients with pancreatitis the RQ did not change significantly after glucose infusion. The calorimetric data obtained during TPN, however, are consistent with the fact that the patients were oxidizing the infused glucose (RQ = 0.90 ± 0.02). Thus, patients with pancreatitis are capable of adaptation to the glucose infusion.

It is unlikely that these patients would have been heavily reliant on FFA oxidation for energy because their rate of FFA turnover was similar to that seen in normal volunteers. In addition, as was seen in the volunteers, there was a significant decrease in FFA turnover when the patients were infused wth glucose. This presumably would have been associated with a decrease in FFA oxidation, as FFA use usually parallels FFA availability.[14] However, the indirect calorimetric data obtained from the pancreatitis patients indicate that the situation concerning total fat oxidation in these patients is a complex one. The basal

value for nonprotein RQ in the patients (calculated using the indirect calorimetry and urea turnover data) was 0.70, indicating a heavy reliance on fat. Thus, it is apparent that although the patients with pancreatitis did not have an increased rate of lipolysis and therefore presumably had no increase in FFA oxidation, they were heavily dependent on fat (presumably intracellular triglycerides) for energy.[18]

In summary, it appears that patients with pancreatitis are metabolically similar to septic patients.[6] Although both groups of patients are less sensitive to the protein-sparing effects of glucose infusion than normal volunteers, 2 hours of glucose infusion significantly reduced their elevated rate of net protein catabolism. In addition, the patients were able to adapt to an increase in glucose availability by increasing the percentage of glucose uptake oxidized during TPN.

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